

**REMARKS**

This Application has been carefully reviewed in light of the Final Office Action mailed December 9, 2005. At the time of the Final Office Action, Claims 138-148 were pending in this Application. Claims 138-148 were rejected. Claims 149-151 were previously cancelled without prejudice or disclaimer. Claims 138 and 148 have been amended. Applicant respectfully requests reconsideration and favorable action in this case.

**Examiner Interview**

Examiner Shibuya kindly granted Applicant's request for a telephonic interview and the interview was held on January 25, 2006. Applicant has received the Examiner's Interview Summary dated February 2, 2006. Applicant offers the following summary of the topics discussed. The order tracks the order of the outstanding Office Action rather than the order actually discussed during the call.

The Examiner's remarks in the outstanding Office Action regarding Applicant's first and second Rule 132 Declarations were discussed. Applicant's Attorney, Dr. Guy Birkenmeier, respectfully asserted that no inconsistency exists between the Declarations, but rather that both unequivocally demonstrate that the compositions of Nakazawa all contain particles, precipitates, or both. Applicant's Attorney explained that the Declarations both demonstrate that Nakazawa does not enable one of ordinary skill in the art to make a solution that is free of precipitates and, therefore, does meet the requirements of 35 U.S.C. § 112, first paragraph. The Examiner stated that the Declarations were not persuasive. Applicant's Attorney asked for an explanation of what fault or weakness existed in Applicant's methods and data. The Examiner said he did not know. Applicant's Attorney then asked what additional experiments could be tried such that the results, if favorable, would fill any perceived gap. The Examiner said he could not think of any such experiments.

Regarding objections to Applicant's attempt to replace "citrate" with "sulfate" in several places in the specification, Applicant's Attorney explained that these changes were simple typographic errors (*e.g.*, cut-and-paste errors) and invited the Examiner's attention to support in the surrounding text. In response, the Examiner kindly indicated that he would seek the opinion of another Examiner as to whether the proposed changes are adequately supported.

Applicant's Attorney, Dr. Guy Birkenmeier, proposed amendments to claims 138 and 148. The Examiner indicated that replacing "of the solution within a selected range of pH values" with "obtainable in an aqueous system" would overcome the rejection under 35 U.S.C. § 112, second paragraph raised against the former language. The impact of the proposed replacement of the term "clear" with "substantially free of precipitates or particles" on the 35 U.S.C. § 112, second paragraph rejection was not discussed.

No agreement was reached on the effect of the proposed replacement of the term "clear" on the rejection over Nakazawa. The Examiner indicated that he was having difficulty understanding solution chemistry and the difference between the compositions of Nakazawa and the instant application. Applicant's Attorney explained that Applicant's Declarations demonstrated that Nakazawa failed to enable preparation of solutions that are substantially free of precipitates or particles.

Finally, Applicant's Attorney respectfully suggested that the chemical and structural differences between cyclodextrins and the disclosed and claimed "aqueous soluble starch conversion product" and "aqueous soluble non-starch polysaccharide" are matters of carbohydrate chemistry of which the Examiner may take official notice. Without disagreeing with this suggestion, the Examiner articulated a preference to have Applicant submit evidence of the differences. Accordingly, Applicant submits herewith McNaught, Lehninger, Horton, and Schmid (Exhibits 33-36). Full citations for these documents may be found in Applicant's Information Disclosure Statement and Form PTO-1449 submitted herewith.

#### **Yoo Declarations I and II Are Consistent**

The second declaration of Seo Hong Yoo submitted under 37 C.F.R. §1.132, was considered by the Examiner but was allegedly ineffective to overcome Japanese Patent No. JP62153220 issued to Shinzo Nakazawa et al. ("Nakazawa"). However, neither the Office Action nor the Examiner Interview identified any credible flaw with the experimental methods or results. The Office Action appears to improperly disregard the teachings of Dasta that visual inspection is a sensitive, art-recognized method of evaluating whether compositions are free of particles or precipitates. In addition, the Office Action alleges that an inconsistency exists between the first and second Declarations. The first Declaration states with respect to Nakazawa's Working Example 1:

Upon heating, the solution with amyloextrin became mostly clear with some undissolved matter. After the solution cooled to room temperature, the solution appeared opalescent or turbid. Declaration dated May 14, 2004, Section 6(A)(i), Page 4.

Thus, the "mostly clear" expression referenced in the Office Action relates to a **heated** composition. Even at elevated temperature though, the composition still included "undissolved matter." Applicant's second Declaration states:

Under my direction and control, the clarity of each solution in Paragraph 5 (above) [describing the preparation of compositions including Nakazawa's Working Example 1 presented in Table 4] was visually assessed within about two days of preparation.. Declaration dated August 2, 2005, Paragraph 7 Page 9.

Thus, observations in the second Declaration were made at ambient temperature. The Office Action's allegation that the Declarations are inconsistent improperly ignores (a) the plain fact that Applicant's first Declaration statement manifestly indicates that the **heated** Nakazawa composition included precipitates and (b) the **consistency** of the observations for compositions at **room temperature**: "opalescent or turbid" in the first Declaration and "opaque (later, opaque jelly formed) in the second Declaration. Accordingly, there is no basis for the skepticism expressed in the Office Action about the credibility of Applicant's methods or the teachings of Dasta.

### **Specification Objections**

The Office Action indicates that the Specification stands objected to under 35 U.S.C. §132(a) because it allegedly introduces new matter into the disclosure. Applicant has amended the specification with respect to the appearance of the terms "aqueous soluble" and "chelate" in the paragraph at Page 53, Lines 1-5. Applicant continues to assert that support exists in the application as filed for the terms "aqueous soluble" and "chelate," but has amended the specification to expedite prosecution.

Further to the Examiner Interview of January 25, 2006, Applicant respectfully requests reconsideration of the replacement of "citrate" with "sulfate" at Page 53, Lines 6-14, Page 53, Line 19, Page 54, Line 10, and Page 55, Lines 1-10.

The Office Action invites Applicant to point to support in the specification as filed for Applicant's amendment replacing "DMT" with "dacarbazine." Applicant respectfully

observes that it is the abbreviation "DTC," not "DMT," that Applicant has sought to expand. Applicant's Attorney has asserted on the basis of information and belief that "Bayer sells dacarbazine under the trade name 'DTC-Dome.'" See Response to Office Action dated August 2, 2005. With respect to this assertion, Applicant respectfully invites the Examiner's attention to the enclosed print-out from NAM, a British charitable organization (Exhibit 1). However, it has now come to Applicant's attention that the National Library of Medicine (Exhibit 2) and the National Cancer Institute (Exhibit 3) both indicate that dacarbazine may be abbreviated "DTIC." Accordingly, Applicant respectfully withdraws this contention and respectfully asserts that it was an error made without any deceptive intent.

Applicant has herein amended "DTC" to recite "diethyldithiocarbamate." Applicant asserts that one of ordinary skill in the art would have understood the abbreviation "DTC" to refer to imuthiol, which is diethyldithiocarbamate, in view of the context in which the expression appeared in the application as originally filed (*i.e.*, immediately following "levamisole") and Neveu (Exhibit 4), Nagy (Exhibit 5), ClinicalTrials (Exhibit 6), and/or Hubner (Exhibit 7). Applicant respectfully invites the Examiner's attention to Neveu, Nagy, ClinicalTrials, and Hubner which clearly indicate that diethyldithiocarbamate may be abbreviated DTC. While Applicant notes that one source indicates that diethyldithiocarbamate may be abbreviated "DDTC" (Exhibit 8), Applicant observes that even this abbreviation contains "DTC." Thus, Applicant's amendment does not constitute new matter and the rejection should be withdrawn.

**Rejection under 35 U.S.C. § 112, First Paragraph**

The Office Action indicates that Claims 145-147 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office Action alleges that attorney argument cannot take the place of objective evidence. Applicant traverses this rejection and respectfully invites the Examiner's attention to documents enclosed herewith as follows:

Claim	Activity	Compound	Document
145	"an agent having anticonvulsant activity"	albuterol sulfate	Proventil (Exhibit 9)
		ethylnorepinephrine	Dorland's (Exhibit 10) Giorgi (Exhibit 11) Bodin (Exhibit 12)
		Albizzia lebbeck	Kasture 1996 (Exhibit 13) Kasture 2000 (Exhibit 14)
146	"an agent capable of prolonging survival time in hypoxic conditions"	UDCA	Paul Pui-Hay But (Exhibit 15) Rajesh (Exhibit 16) Rodrigues (Exhibit 17)
		hydralazine	Drug Information: Hydralazine (Exhibit 18)
		isoxsuprine	Drug Information: Isoxsuprine (Exhibit 19)
		nylidrin	Drug Information: Nylidrin (Exhibit 20)
		dyphylline	Drug Information: Dyphylline (Exhibit 21)
		pirbuterol	Drug Information: Bronchodilators, Adrenergic (Exhibit 22)
		colfosceril palmitate	Tiscali (Exhibit 23)
		selenium	Selenium (Exhibit 24)
147	"an agent capable of alleviating or ameliorating a condition selected from the group consisting of stomatitis, gingivoglossitis and toothache"	UDCA	LG Household (Exhibit 25)
		acyclovir	Zovirax (Exhibit 26)
		penciclovir	Denavir (Exhibit 27)
		colchicine	Fontes (Exhibit 28)
		celecoxib	Drug Information: Celecoxib (Exhibit 29) Wynn 2002 (Exhibit 30) Wynn 2002 (Exhibit 31)
		codeine methadone morphine ibuprofen naproxen	Preshaw (Exhibit 32)

In providing these documents, Applicant has provided ample evidence that the recited compounds have an activity corresponding to claims as indicated. These activities, in turn, adequately describe the genera claimed. With respect to claim 147, Applicant also respectfully invites the Examiner's attention to the specification as originally filed at Page 20, Lines 7-11, where mouthwash formulations are disclosed and at Page 25, Lines 13-17, where anti-inflammatory drugs and anesthetics are disclosed. These disclosures clearly demonstrate applicability to dental and/or oral care. For these reasons and the reasons already of record, claims 145-147 are fully supported by the specification as filed. Withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. § 112, Second Paragraph**

The Office Action indicates that Claims 138-148 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant amends Claims 138 and 148 to replace the expressions "clear" and "of the solution within a selected range of pH values" with "substantially free of precipitates or particles" and "obtainable in an aqueous system," respectively. Accordingly, Applicant respectfully requests withdrawal of these rejections.

**Rejection under 35 U.S.C. § 102: Nakazawa**

The Office Action indicates that Claims 138-141 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Japanese Patent Application Publication No. 62153220, formal translation, by Shinzo Nakazawa and Satoshi Hisano ("Nakazawa"). Applicant respectfully traverses and submits the cited art does not teach all of the elements of the claimed embodiment of the invention. More specifically, Nakazawa fails to provide an enabling disclosure of compositions that are "substantially free of precipitates or particles."

According to the Federal Circuit, "[t]o serve as an anticipating reference, the reference must enable that which it is asserted to anticipate." See e.g., *Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education and Research*, 346 F.3d 1051, 1054, 68 U.S.P.Q.2d 1373, 1375-1376 (Fed. Cir. 2003). For a reference to anticipate, it must not only teach each and every element of the claimed invention, but must also enable the artisan of ordinary skill to make and use the claimed invention without undue experimentation. See

*e.g., PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 U.S.P.Q.2d 1618, 1624 (Fed. Cir. 1996); *Minnesota Mining and Manufacturing Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301, 64 U.S.P.Q.2d 1270, 1278 (Fed. Cir. 2002); *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1369, 52 U.S.P.Q.2d 1129, 1134 (Fed. Cir. 1999).

The Office Action indicates that Applicant's Declaration dated August 2, 2005 is not found persuasive. The Office Action's position, as discussed in the foregoing section, appears to be based on an alleged inconsistency between Applicant's first and second Declaration with respect to the results obtained with Nakazawa's Working Example 1. Applicant maintains, as explained herein, that no such inconsistency exists. The first and second Declarations both report the appearance of compositions prepared according to Nakazawa's Working Example 1 as opaque when the compositions are at ambient temperature. Only Declaration I expressly reports the appearance at elevated temperature and even then, the composition was observed to have precipitates.

The Office Action also faults Applicant's argument for allegedly being directed to limitations not recited by the pending claims. The Examiner indicated in the Interview Summary mailed February 2, 2006 that "amendments to the instant product claims, which provided structural limitations that distinguished over the prior art, would better serve to show in what manner that the compositions taught by Nakazawa are different from applicant's claimed invention." Applicant has herein amended Claims 138 and 148 to recite "substantially free of precipitates or particles" and contends that this constitutes a "structural" difference between the compositions of Nakazawa and the compositions disclosed by the instant application. Moreover, Applicant has provided ample evidence that Nakazawa's disclosed methods, which differ from Applicant's disclosed methods, fail to enable one of ordinary skill in the art to make compositions that are "substantially free of precipitates or particles." Under Federal Circuit law, therefore, Nakazawa cannot anticipate the instant claims. Accordingly, Applicant respectfully requests withdrawal of this rejection.

#### **Rejection under 35 U.S.C. § 102: Panini**

The Office Action indicates that Claims 138-141 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by *Improvement of Ursodeoxycholic Acid Bioavailability by 2-Hydroxypropyl-β-Cyclodextrin Complexation in Healthy Volunteers*, by R. Panini et al., Pharmacological Research, Vol. 31, No. 3/4, 1995 ("Panini"). Applicant

respectfully traverses and submits the cited art does not teach all of the elements of the claimed embodiment of the invention.

Regarding starch conversion products and non-starch polysaccharides disclosed, for example, at pages 22-23 of the instant application, Applicant respectfully invites the Examiner's attention to the entire disclosures of McNaught (Exhibit 33), Lehninger (Exhibit 34), and Horton (Exhibit 35). Applicant respectfully invites the Examiner's attention to McNaught Section 37.2 (Page 1992 *et seq.*), Section 37.4 (Page 1994 *et seq.*), and Section 38.2 (Page 1996). Applicant respectfully invites the Examiner's attention to Lehninger Sections 7.1 and 7.2 and Figures 7-5, 7-11, and 7-15. Applicant respectfully invites the Examiner's attention to Horton, Section 8.5(B). With respect to cyclodextrins, Applicant respectfully invites the Examiner's attention to the entire disclosure of Schmid (Exhibit 36). As exemplified by the disclosures of McNaught, Lehninger, Horton, and Schmid, numerous differences exist between the geometric, physical, and chemical properties of cyclodextrins and starch conversion products and non-starch polysaccharides disclosed by the instant application.

Applicant continues to respectfully contend that Panini fails to teach or suggest "a second material selected from the group consisting of an aqueous soluble starch conversion product, an aqueous soluble non-starch polysaccharide, and combinations thereof." In addition, Applicant respectfully invites the Examiner's attention to Panini at Page 202, left column where Panini clearly discloses that it relates to formulation of tablets. Nowhere does Panini teach or even suggest a solution that is "substantially free of precipitates or particles." Accordingly, Panini fails to anticipate the instant claims for failing to disclose at least these limitations. Applicant, therefore, respectfully requests withdrawal of this rejection.

#### **Rejection under 35 U.S.C. § 102: Widauer**

The Office Action indicates that Claims 138-141 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,534,505 issued to Josef O. Widauer ("Widauer"). Applicant respectfully traverses and submits the cited art does not teach all of the elements of the claimed embodiment of the invention. Specifically, Widauer fails to teach or suggest a solution that is "substantially free of precipitates or particles." On the contrary, crystals are disclosed as being desirable to overcome the bitter taste of bile. *See e.g.* Widauer, col. 1, lines 62-67 ("...contains the active agent [UDCA] **mainly** in a fine



crystalline form...")(emphasis added). In addition, Widauer fails to teach or suggest "a second material selected from the group consisting of an aqueous soluble starch conversion product, an aqueous soluble non-starch polysaccharide, and combinations thereof." Since Widauer fails to teach every element of the pending claims, it cannot anticipate those claims. Accordingly, Applicant respectfully requests withdrawal of this rejection.

**Rejection under 35 U.S.C. § 102: Ventura**

The Office Action indicates that Claims 138-141 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by *Improvement of Water Solubility and Dissolution Rate of Ursodeoxycholic acid and Chenodeoxycholic acid by Complexation with Natural and Modified  $\beta$ -cyclodextrins*, by C.A. Ventura et al., International Journal of Pharmaceutics, Vol. 149, pp. 1-13, 1997 ("Ventura"). Applicant respectfully traverses and submits the cited art does not teach all of the elements of the claimed embodiment of the invention. Specifically, Ventura fails to teach or suggest a solution that includes "a second material selected from the group consisting of an aqueous soluble starch conversion product, an aqueous soluble non-starch polysaccharide, and combinations thereof." Since Ventura fails to teach every element of the pending claims, it cannot anticipate those claims. Accordingly, Applicant respectfully requests withdrawal of this rejection.

**Rejections under 35 U.S.C. §103: Nakazawa and Acharya**

Claims 138-147 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Nakazawa and U.S. Patent No. 6,210,699 issued to Ramesh N. Acharya et al. ("Acharya"). Applicant respectfully traverses and submits the cited art combinations, even if proper, which Applicant does not concede, does not render the claimed embodiment of the invention obvious. Nakazawa fails to enable preparation of a composition that is "substantially free of precipitates or particles." Acharya fails to teach a composition that is "substantially free of precipitates or particles." Therefore, at least for this reason, Nakazawa and Acharya, whether considered alone or in combination, fail to teach or suggest every limitation of the instant claims. Accordingly, Applicant respectfully requests withdrawal of this rejection.

**Rejections under 35 U.S.C. §103: Nakazawa and Vandelli**

Claim 148 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Nakazawa and *2-Hydroxypropyl- $\beta$ -Cyclodextrin Complexation with Ursodeoxycholic Acid*, by M.A. Vandelli et al., International Journal of Pharmaceutics, Vol. 118, pp. 77-83, 1995 ("Vandelli"). Applicant respectfully traverses and submits the cited art combinations, even if proper, which Applicant does not concede, does not render the claimed embodiment of the invention obvious. Nakazawa fails to enable preparation of a composition that is "substantially free of precipitates or particles." Vandelli fails to teach a composition that is "substantially free of precipitates or particles." Therefore, at least for this reason, Nakazawa and Vandelli, whether considered alone or in combination, fail to teach or suggest every limitation of the instant claims. Accordingly, Applicant respectfully requests withdrawal of this rejection.

**CONCLUSION**

Applicant has now made an earnest effort to place this case in condition for allowance in light of the amendments and remarks set forth above. Applicant respectfully requests reconsideration of the pending Claims.

Applicant encloses a Request for Continued Examination (RCE) and a check in the amount of \$395.00 for the RCE fee. Applicant believes there are no further fees due at this time, however, the Commissioner is hereby authorized to charge any fees necessary or credit any overpayment to Deposit Account No. 50-2148 of Baker Botts L.L.P.

If there are any matters concerning this Application that may be cleared up in a telephone conversation, please contact Applicant's attorney at (512) 322-2647.

Respectfully submitted,  
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- Enclosures:
- 1) Request for Continued Examination (RCE) and a check in the amount of \$395.00.
  - 2) An Information Disclosure Statement and PTO 1449 form with copies of the references and a check in the amount of \$180.00.
  - 3) Change of Correspondence Address